SPACE GASTROENTEROLOGY

A Review of the Physiology and Pathology of the Gastrointestinal Tract as Related to Space Flight Conditions

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CONTENTS

INTRODUCTION

Interest for many years in the possibility of manned space flight has finally culminated in the successful flights of Project Mercury, Project Gemini, and various Soviet excursions, and in the preparation of future extended orbital, lunar, and Martian voyages. Coincident with the progress in engineering technology associated with space flight, the field of aviation medicine has enlarged to that of aerospace medicine. Thus, in its current state of the art, the discipline of aerospace medicine encompasses the problems and knowledge of conventional aviation medicine, the information gained from simulated and preliminary, brief space excursions, and the speculations of biomedical phenomena of space flight which are generally ground-based and conjectural. It is in the less developed area of aerospace medicine, associated with extended space flight, that the field of space gastroenterology is emerging. Although gastroenterology is commonly associated with the clinical diagnosis and treatment of gastrointestinal disorders, the domain of "space gastroenterology" falls within the broader definition of the term, and concerns primarily the study of normal and abnormal gastrointestinal function under the imposition of space flight conditions, as well as the preventive, minor therapeutic, and life support measures taken to maintain normal gastrointestinal function during space flight. Therefore, like the other categories of aerospace medicine (which is itself a subspeciality of preventive medicine), space gastroenterology is primarily in the realm of preventive and experimental medicine.

As is the case with most of the other physiologic systems which present aerospace medical problems, the gastrointestinal tract is influenced by most of the environmental stresses incurred during space flight. Thus, the following paragraphs delineate the stressors an astronaut encounters during flight which may influence his gastrointestinal tract; these include acceleration stress, vibration, weightlessness, radiation, altered environmental gas composition and pressure, chronic restraint and lack of exercise, feeding and defecation problems, and physiological and psychological fatigue.

LINEAR AND ANGULAR GRAVITATIONAL STRESS

Experiments with both man and animals that involve alterations in rate of motion (linear and angular acceleration and deceleration) and constant G-stress (centrifugation) have indicated that these stressors can induce gastrointestinal changes which may be deleterious. Britton and coworkers (1) found during their extensive centrifugation research that positive G-stress inhibited gastric emptying time in cats. By means of barium sulfate test meals, they observed gastric emptying delays of approximately 2 hours following exposure to 2.7 G (1-4 min.) and of 6-7 hours following 6.2 G for 3 min. Similarly, Suvorov recently reported (2) that centrifugation (3-5 G for 30 sec.) produced an inhibition of gastric secretion in human subjects for 10-30 min. followed by a sharp increase in secretory activity. The increased secretion was generally characterized by increases in free and total acidity and peptic activity of gastric juice. Suvorov found no change in the periodic contractions of the stomach following centrifugation, and observed no effect on the gastric response to angular acceleration following repeated accelerations at intervals of 5-6 days. Bonner (3) also reported an inhibitory effect of centrifugation on gastric secretion. In his study of 23 human subjects exposed to prolonged positive G-stress, he noted increased uropepsin excretion in urine of subjects just prior to the test (presumably due to psychic stimulation), followed by decreased uropepsin excretion during centrifugation. Deprivation of visual and auditory stimuli did not produce any significant change in uropepsin excretion from the pretest elevated levels.

Khazen and Vaysfel'd (4) recently reported that the histamine content of intestinal mucosa of rats increases following single, positive, radial accelerations, but decreases following single, negative, radial accelerations. They further noted, in contrast, that intestinal histamine decreases following multiple and frequently repeated positive accelerations. Although it is difficult to interpret the significance of their finding, an increase in the histamine content of mucosal tissue may be considered potentially hazardous. Indeed, various investigators, (5-7) have demonstrated that histamine releasers, such as compound 48/80 and polymyxin B, produce acute gastric hemorrhagic necrosis of the mucosa only a few hours after a single intraperitoneal injection in the rat. In addition, exogenous histamine is a well-known secretogogue and is frequently associated with gastric ulcerogenesis. The vascular response (reduced blood flow, stagnant anoxia, etc.) of the splachnic area following administration of exogenous histamine is generally regarded as an important etiological factor in post-histamine ulceration of the stomach.

Severe gastric injury has been observed in black bears subjected to abrupt, linear deceleration trauma. Bears have been utilized for viseral displacement studies on rocket propelled sleds since they approximate man's conformation and weight, and stand upright easily, with the head at a normal inclination. Cook and Mosely (8) reported small longitudinal tears along and across the fundic mucosa, and congestion and hemorrhage of the serosa of stomachs of bears which were subjected to 73-96 G (linear deceleration) in 0.024 second. These lesions were attributed to distortion and stretching of the stomach following upward visceral displacement toward the diaphragm. Similarly, Hershgold (9) illustrated by abdominal roentgenograms the vulnerability of mediastinal and abdominal organs to forward acceleration (6-12 G) and to left and right sideward accelerations (6 G) in human subjects. Deleterious effects such as contusions, lacerations, and rupture of internal organs, especially in hollow fluid-containing organs, have been observed following compressive and shearing stresses and strains arising from blows to various parts of the body (10). However, studies with mice (11) have indicated that the lungs, liver, spleen, and mesentery were most frequently affected by large forces applied transversely (abrupt linear deceleration) through the body.

In conjunction with visceral displacement problems, early workers have shown that cats exposed to high decelerative forces show increased intra-abdominal pressure (12). Clark and Jorgenson (13) reported that humans given 1.5-2.0 liters of water, milk, or a heavy meal prior to angular acceleration (3 G for 15 sec.) showed increased tolerance to the centrifugation, which they attributed to the increased intra-abdominal pressure resulting from the ingestion of bulky material. This is in agreement with the well-known increase in G tolerance provided by pressurized abdominal belts and bladders in antiblackout suits which also increase intra-abdominal pressure. Increased tolerance to G stress resulting from filling the stomach with water has also been observed by Browne (14).

As indicated above, the stresses imposed upon mammalian organisms by abrupt and/or intense acceleration or deceleration (linear or angular) can induce severe gastrointestinal disturbances. However, these factors are not limiting for space flight, since 1, high G stress is limited to relatively short periods of take-off and reentry of the space vehicle, 2, space flight personnel will be optimally positioned during the short durations of take-off and reentry, 3, maximum G stresses will be kept within tolerance limits, and 4, within certain limits space flight personnel can be screened for susceptibility and conditioned for tolerance to the above stresses. Nevertheless, adverse motion effects on gastrointestinal function in some space excursions might be encountered. Personnel in rotating space platforms will encounter Coriolis effects, which may induce autonomic effects leading to adverse gastric symptoms and reflex vomiting. Gray et al. (15) reported intense motion sickness symptoms in subjects of visual studies of Coriolis effects, although more recent work by Stewart and Clark (16) failed to incriminate Coriolis effects in the induction of "stomach awareness" or motion sickness. Numerous studies have shown that pilot experience is beneficial in decreasing the susceptibility to motion sickness induced by rotation (17).

VIBRATION

For many years both experimental studies and uncontrolled observations have shown the association of vibration stress with adverse physiologic effects. Early vibration experiments in aviation were usually related to the influence of high frequency vibration of aircraft motors on the pilot, air-crewmen, and passengers. However, current studies are attempting to delineate the effects of low frequency, high amplitude vibrations since the latter are observed in high speed, low altitude flights (buffeting), and appear to be of vital importance in the launch and reentry phase of rocket propelled, manned space vehicles (18). Undesirable gastrointestinal symptoms induced by vibrational stress are frequently reported.

Animal Experiments

One of the earliest reports (1938) in regard to the gastroenterologic effects of vibration indicated that fecal output increased and that food intake decreased following experimental vibration (unspecified type) of animals (unspecified species), an observation which implied increased intestinal motility and/or decreased absorption (19). During the following two decades there were no reports in the literature in this regard until the communication of Roman (20), who reported the effects of severe whole body vibration on mice. Roman observed gastrointestinal bleeding in vibrated (5-50 cps) mice, which was especially prominent in the upper half of the small intestine. Photographs of his vibration experiments suggest that the hemorrhage was initiated by the shearing forces induced by extreme displacement of abdominal contents.

Schaefer et al. (21) recently confirmed the observation of Roman and found increased fecal output and decreased food intake in rats during the post-vibrational (25 cps, 0.25 in., 15 min.) period. They reported a normal histology of stomachs and intestines of vibrated, 135-140-day-old rats. However, in an associated study (22) they occasionally noted gastrointestinal tract hemorrhage in 75-day-old rats vibrated at 25 cps, but not in those vibrated at 30-35 cps. Although their study involved only a small number of animals, the differential gastrointestinal effect at 25 cps versus 30-35 cps was marked.

The effect of altitude upon the tolerance to vibration stress in rats was investigated by Megel et al. (23). It was apparent from their observations that vibration (60 cps) increased the lethality rate of altitude stress, the latter which was deleterious primarily through the reduced partial pressure of oxygen rather than through reduced barometric pressure. Severe intestinal hemorrhage occurred in those animals which succumbed to the vibration-altitude environment. Since intestinal hemorrhage and ulceration are usually observed in terminal stages of intense, systemic stress, the conclusion should not necessarily be drawn that the enteric pathology observed by these investigators resulted from specific vibration characteristics.

Human Experiments

Prior to the controlled endeavors designed to delineate the hazardous effects of vibration stress in humans, reports appeared (24,25) which incriminated truck, tractor, and automobile vibration as the cause of gastric upsets. Subsequently, several controlled studies have been undertaken, and a recent review (26) outlines the mechanical vibration effects on human beings. One of the early reports (27) indicates that vibration of man at 25 cps for 15 min. can induce severe harm to the gastrointestinal tract. A human test subject vibrated at these conditions developed moderately severe gastointestinal bleeding which lasted for several days. Other human experiments (28) demonstrated that abdominal pain occurred during vibration at 3, 4, and 6-10 cps. The pain had a slow onset, was dull and aching in nature, was similar to "gas pains," and was especially prominent at 6 cps. Ziegenruecker and Magid (28) believe that the pain was caused by the stretching of the terminal ileum, cecum, and hepatic flexure of the large intestine and its supporting mesentery. Markaryan (29) and Guignard (30) also observed abdominal pain in human subjects vibrated at 10, 40, and 70 cps, and 6-12 cps, respectively. Magid and Coermann (31) reported abdominal pain at 4-14 cps vibration, and a defecation urge of human subjects vibrated at 9-20 cps. Recently, Chaney (32) reported abdominal pain at 4-12 cps, flatus passing at 18-24 cps, and defecation urge at 16-27 cps in human subjects. In addition, excessive noise (vibration in the audible range) has been involved in the etiology of nausea and vomiting (33), and in the pathogenesis of dyspepsia and duodenal ulcer (34).

It can be concluded that short-term vibration, particularly at levels of 25 cps or lower, is capable of inducing abdominal pain, gastrointestinal hemorrhage, and defecation urge in humans. Since low frequency, high amplitude vibration is encountered in certain phases of rocket flight, it is imperative to control both the duration and intensity of vibration therein. Additional investigations 1, to evaluate human tolerances further, 2, to devise dampening restraint chairs and suits, and 3, to assess individual susceptibilities to vibration are required to minimize gastrointestinal manifestations of vibration.

INGESTION AND EGESTION

The problems of ingestion and egestion during space flight involve phenomena at the two extreme ends of the gastrointestinal tract, thus, feeding and defecation processes relate to both the internal physiology and the external environment, and require the cooperative effort of the space gastroenterologist, the space nutritionist, and the life support engineer.

The fact that feeding during short-term aircraft flights offers no problem is manifested by the thousands of conventional meals served by commercial airlines during flight. Feeding during long-range military flights poses problems in that pressure suits hamper defecation procedures. Thus, B-66 crews which participate in long-range over-water missions generally subsist on very low residue diets for 72 hours prior to take-off (35). Also, the use of liquid foods has been found to be a feasible method of feeding for pilots of long-range jet fighter missions (36). Although preliminary manned space flights have also involved the gastrointestinal, preflight conditioning of astronauts by feeding of low residue diets, and have utilized packaged meals of low residue content, extended space voyages of days and weeks cannot be met with such an easy solution. The problems of space nutrition have been reviewed elsewhere (37-41), and pose such problems as the determination of caloric requirements for weightlessness conditions, the selection of foods, which are both palatable to individual astronauts and suitable for freeze-drying, and the fabrication of food containers which are transparent, durable, and waterproof, and perhaps edible. The fact that all problems cannot be solved in the laboratory is illustrated by the water leakage from the food bags reported by Major Gordon Cooper during his flight (42), and the softened and melted foods tested by Astronaut Carpenter (43). It appears that extended space flights will eventually require closed food cycles; thus numerous synthetic diets have been proposed (44). However, missions undertaken during the next 20 years will most likely carry food from earth in dehydrated or frozen forms (45).

Various methods have been proposed for waste management aboard space vehicles or stations. Alternatives include drying fecal matter by heat or dry air, macerating and pressure filtering waste products, or utilizing a self-perpetuating biological regenerative system. The latter method seems most feasible for extended space flights; with a typical activated sludge (mixed microbial population of bacteria, fungi, protozoans, and high organisms) process, efficiencies of 95-98 percent are obtainable, taking care of all waste products, including feces, urine, and garbage (45). Current research in this area is under way, involving investigations of anaerobic and aerobic systems. For medium-length voyages incineration may ultimately prove to be the best method of disposal of feces, while collection and storage of waste products in impermeable plastic bags can suffice for missions of short duration.

WEIGHTLESSNESS

The influence of weightlessness on gastrointestinal function has not yet been fully assessed, although preliminary, short-term space flights have included feeding schedules for astronauts and cosmonauts. Inasmuch as prolonged weightlessness cannot be simulated in the laboratory, only speculation can be made as to the influence of weightlessness on gastrointestinal function. Laboratory studies have shown, however, that subgravity conditions produced by the "subgravity tower" in Rome have produced displacement of thoraco-abdominal viscera of human test subjects (46). Previous space flights have indicated that normal esophageal reflexes occur during weightless conditions following mechanical stimuli of food boli.

However, space flights of longer duration are required to assess the movement and digestion of food in the lower digestive tract, and particularly to assess defecation problems. It has been speculated (47) that the weightlessness of the food eaten by the Soviet Cosmonaut, Gherman S. Titov, may have caused the illness he reported in his 25 hour flight. It is felt that the weight of food and liquids normally plays an important role in their passage from the fundus to the pylorus of the stomach since perestalsis _per se_ is not considered to take place in the upper stomach (48). Until more information is obtained in regard to the effect of weightlessness on gastrointestinal motility, and food passage, the provision of space flight personnel with parasympathomimetic or anticholinergic agents has been recommended (48). Adequate exposure of food to gastric juices in the stomach also may fail to take place if the food is weightless. At the anterior aspect of the digestive tract three additional problems might be encountered: 1, there might be increased aerophagia, resulting in flatulence, 2, voluntary, or reflex eructation of air, which normally gravitates toward the cardiac sphincter, might be hindered by weightlessness, also resulting in flatulence, and 3, increased exposure of the cardiac sphincter and lower esophagus to acid peptic secretions, which normally are shielded to some degree by the air pocket which gravitates to this region when the body is in an upright position, might occur and induce reflux esophagitis. At the distal end of the digestive tract other problems might occur (37); the entrapped gas bubbles (nitrogen, carbon dioxide, methane, etc.) might not coalesce in the terminal portion of the large bowel due to weightlessness of solid fecal material. As a result, reflexes which normally activate the anal sphincter might become incoordinate in regard to selection of passage of gas or gas-impregnated fecal matter.

FATIGUE

Although personnel of spacecraft and orbiting laboratories will have work, relaxation, and sleep schedules which should allow adequate rest, especially during extended voyages, the mental strain, isolation, and complexity of the situation will undoubtedly present situations which predispose fatigue symptoms. Indeed, the peculiar professional syndrome well-known in aviation medicine as "pilot fatigue," and which appears in personnel of long lasting, stressful flight activities (49,50), can be anticipated in space flight. This phenomenon can be complicated further by long and delayed countdowns prior to launching, by extensive preflight preparation, and by inadequate sleep due to preflight anticipation. The alimentary tract in many persons is more sensitive to stressful influences than any other part of the body, and fatigue from any cause is likely to interfere with the digestive processes (51,52). A recent survey (53) involving 61 recognized gastroenterologists indicated that 52 percent of the gastroenterologists thought ulcerogenesis resulting from the stresses of space flight "should be considered a real threat to the success of space travel." Alvarez has cited numerous examples of digestive disturbances resulting from fatigue: inhibition of gastric secretion has been demonstrated in man during states of exhaustion; and nausea, abdominal cramps, flatulence, and diarrhea have been observed in persons who eat heavily while extremely tired (54). In addition, Rehfuss (55) noted anorexia, indigestion, and atony of the stomach in the presence of muscular fatigue. Recently Oliver (56) reported disturbances (flatulence, nausea, belching, anorexia, abdominal distention, constipation, heartburn, abdominal cramps, and vomiting) of the gastrointestinal tract in 57 percent of 100 ambulatory patients under treatment for chronic fatigue.

The various gastrointestinal pathologies resulting from stress have been reported by Selye in his classic paper (57), have been reviewed by Paulley (58), and range from spastic colon and gastric ulcer to acute appendicitis and scleroderma. Significant increases in gastric hydrochloric acid secretion during experimentally produced chronic fear in dogs and monkeys (59) and during sustained "examination-period anxiety" in undergraduate students have been observed (60). Gray and his associates (61) propose that chronic stress, acting through the pituitary-adrenal mechanism, increases gastric acid secretion, and thus plays an important role in the etiology of peptic ulcer. Numerous investigators, including the writer (62), have shown that administration of exogenous but natural corticoids can be ulcerogenic. Furthermore, Woldman (63) has demonstrated a striking correlation between the severity of adrenal damage, as found in microscopic studies, and the incidence of acute ulceration of the upper gastrointestinal tract. Since Murphy (64) has reported that the corticoid excretion/body surface area ratio increased in jet pilots during flights, it may be anticipated that similar increases in adrenal activity might occur during space flights. Thus, gastrointestinal function may be influenced secondarily to endocrine function during space flight.

Although the terms "chronic fatigue," "chronic anxiety," and "psychological stress" are treated ambiguously in the literature, the close relationship of these states with one another, and with physiological stress symptoms including gastrointestinal manifestations, is readily apparent. Since the syndromes of diarrhea, vomiting, abdominal pain, and particularly ulcer formation represent medical problems of considerable concern they must be considered in the preparation of spacecraft life support and medical systems. The environmental and psychological stress cannot be eliminated, especially in extended voyages. Thus, gastrointestinal functional tests and adrenocorticoid response tests may prove beneficial in selection of astronauts, when used in conjunction with psychological testing and conditioning regimens.

ENVIRONMENTAL GAS PRESSURE

Among the numerous physiological problems related to alterations in total atmospheric pressures, the problem of abdominal gas distention at altitude has long been appreciated in aviation medicine. In a manner analogous to balloon expansion at high altitude, the gastrointestinal gases which are trapped in the gut lumen by partially digested food and fecal material, and which are bounded by the elastic limits of the enteron and abdomen, expand in inverse proportion to the atmospheric pressure outside the body. The average abdominal gas content of young men of average weight (150 lbs.) is about 1300 cc. (65). The volume of gas in the stomach or intestine at ground level is approximately doubled at 15,000 feet, increased 3.0 times at 25,000 feet, 5.4 times at 35,000 feet, and 7.6 times at 40,000 feet (66).

Early reports have indicated that pain due to flatulence at altitude is not uncommon. In 110 simulated flights at 35,000 feet, Blair and his associates (65) noted severe discomfort due to gas distention in 5.5 percent, moderate discomfort in 3.6 percent, and slight discomfort in 19.0 percent of their human subjects. They found no consistent change of gas content with time of day or after meals. Taylor and Robinson (66) also reported painful flatulence due to real and simulated altitude (30,000 feet), but found a positive correlation between flatulence and fullness of the stomach with food. The problem of painful abdominal distention has been reviewed by Adler and Grodins (67). They reported that the incidence of abdominal symptoms is higher in the heavier weight group (160-200 lbs.) and the older age group 28-47 yrs.), and that three types of dietary factors may be important in abdominal stress at altitude: 1, gas-forming foods (carbohydrates, milk, etc.), 2, gastrointestinal irritants such as melons, cabbage, spices, etc., and 3, foods to which the individual may manifest an allergic reaction.

The response of gastric acid secretion to distention at altitude has been reported by Danhof and Steggerda (68). They observed that gaseous distention of the stomach is effective in stimulating gastric acid secretion in humans. Mechanical distention of the stomach has long been known to involve the release of gastrin from the pyloric antral mucosa (69), and it has recently been shown (70) that fundic stimulation may result in gastric acid secretion by a vaso-vagal reflex.

The influence of simulated altitude on gastrointestinal motility has also been investigated by McDonough (71) and Steggerda et al. (72). Although the former investigator found no difference in the gastrointestinal transit times of barium sulfate in humans at 38,000 feet or ground level, the latter investigators observed marked increases in colonic activity in human subjects at simulated altitude (12,000 feet). Steggerda and his associates attributed the increased colonic activity to the stimulation by gaseous distention.

It can be anticipated that gastrointestinal symptoms due to reduced pressure, which was of frequent concern in aviation medicine, will be of minor consequence in space travel, since the use of fully-pressurized suits and pressurized cabins will be employed. Rapid decompression in the space environment will obviously be catastrophic to the mission, but inadvertent, partial decompression in a "shirt sleeve environment" of a space capsule could induce abdominal symptoms. Since experience at altitude can increase the tolerance to these symptoms (67), it may be of remote advantage to condition subjects in this manner.

HYPOXIA AND OXYGEN TOXICITY

In conjunction with the effect of altitude and its accompanying decompression on gastrointestinal function, the physiological effects of lowered partial pressures of oxygen at altitude have been a subject of concern for many years. The extensive work of Van Liere, Northup, Nimeh, and others on the influences of hypoxia ("anoxia") on the alimentary tract has been summarized (73). Reports have indicated that 1, lowered oxygen tension (53 mm Hg) temporarily accelerates gastric emptying time in rats, but may prolong gastric emptying in humans, 2, low oxygen pressures depress the secretion of hydrochloric acid in the stomach of man, and 3, low oxygen pressures depress intestinal absorption of sodium chloride, glucose, glycine, but increase intestinal absorption of water. Furthermore, at high altitude (3,000 - 5,000 meters) there seems to be a great predisposition toward gastric and duodenal ulcer as seen in South American Indians (74,75). Presumably the vascular and blood factors play a major role in the etiology and pathogenesis of ulcer at altitude.

Although the problems of impaired gastrointestinal function following hypoxia can be assessed as generally not serious (indeed, hypoxic conditions are not anticipated in space capsules), the gastrointestinal manifestations of prolonged exposure to high oxygen tensions may be of considerable concern. At the present time there is a paucity of information on the pathologic effects of chronic exposure to high partial pressures of oxygen, especially in regard to the alimentary tract. Since 1, the gastrointestinal tract responds readily (ulceration, increased motility, etc.) to general, systemic stresses imposed by severe environmental conditions, 2, gastric and duodenal ulceration have been associated with pulmonary emphysema (76,77,78) the latter syndrome which can be a consequence of oxygen toxicity, and 3, if the atmospheric environment of space vehicles contain high oxygen tensions, it will be necessary to assess gastrointestinal effects of prolonged exposure to high oxygen tensions.

THERMAL STRESS

The influence of heat on gastrointestinal function has been investigated for a number of years. Attempts to study the effects of thermal stress have included experiments with 1, focalized application of heat directly to the gastrointestinal mucosa or exterior gastric surface of animals, 2, generalized application of heat directly to the gastrointestinal tract by ingestion of hot foods in man and animals, 3, placement of men or animals in heated environments, and 4, application of electromagnetic fields to the gastrointestinal tracts of animals to produce heat in local regions by hysteresis.

Internal thermocautery of local regions of the gastric mucosa was first accomplished by Williams (79), who produced lesions in guinea pigs and rabbits with heated metal instruments. Later, Skoryna et al. (80), Williams (81), Phillips et al. (82), and Torgersen (83) produced gastric lesions in similar experiments with rats and guinea pigs. Several months ago Myren and Torgersen (84) reported that application of a heated (55° C) copper rod for 15 seconds to the gastric mucosa of mice decreased the parietal cell succinic dehydrogenase activity, caused an increase in pH of gastric contents, and induced superficial ulceration of the gastric mucosa.

Application of heat to the stomach and duodenum by ingestion of heated foods and fluids has reportedly produced adverse effects on these organs. Decker (85) and Ivy (86) induced gastric lesions in dogs by feeding hot

(70° C) fluids. Eberhard (87) reported no variation in the gastric emptying time in women who were fed coffee heated at 45°-65° C. The suggestion that heat is involved in the etiology of chronic gastritis, peptic ulcer, and particularly in the etiology of gastric carcinoma was advanced by Davis and Ivy (88). The most recent reports concerning the effects of feeding hot foods on human gastric and duodenal function (89-90) have not indicated any deleterious effects from 47°-50° C water ingestion.

Hyperthermic environments have occasionally been used during gastrointestinal experiments (91). Sleeth and Van Liere (92) reported that an environmental temperature of 32° C caused an increase of 10 percent in the gastric emptying time of dogs. In addition, Rafferty and MacLachlan (93) observed that high environmental temperatures depressed the absorption of glucose in the intestines of rats.

The induction of increased temperature by hysteresis has been experimentally employed with rabbits (94). Shorey and coworkers have thus produced intracorporeal hyperthermia by applying electromagnetic fields over organs containing particulate permanent magnetic iron oxide in the circulating blood. They reported that necrosis of the bowel resulted from organ heating (47° C) by this method.

From the foregoing paragraphs it is obvious that increased temperature can induce adverse changes in the gastrointestinal tract, particularly when heat is applied in an intense and localized fashion. However, under space flight conditions problems of hyperthermia will be limited to environmental temperature extremes, and the ingestion of overheated foods is not anticipated. Environmental temperatures may be high during reentry but since these periods will be of relatively short duration, and will not coincide with feeding schedules, the delayed gastric emptying and other changes which may occur should not be considered important.

CHRONIC RESTRAINT AND EXERCISE LACK

During space missions the crew of the vehicle will not only be isolated and separated by hundreds of thousands of miles from their homeland, but will be physically restricted to the small confines of their spacecraft. The deleterious effects of chronic lack of exercise on muscular development and mineral metabolism have long been recognized. However, the influence of chronic restraint (with concomitant lack of exercise) on gastrointestinal function has not been evaluated. Numerous studies (95-99) have been directed, on the other hand, toward elucidating the effects of exercise on gastrointestinal function. This problem has been reviewed by Stickney and Van Liere (100). In general it may be concluded that mild exercise such as walking is usually without influence on the stomach contractions, though occasionally it may be stimulating. Severe and exhausting exercise usually depresses gastric secretion and motility in man (100) and animals (97-99). Information gained from these studies, however, is of little value in the prediction of the influence of chronic exercise lack on gastrointestinal function. Similarly, previous reports in regard to the influence of restraint on gastrointestinal pathology (101-114) are not applicable to this problem since 1, they are limited to very acute restraint periods (24-48 hours, or intermittent 4-hour periods), and 2, they involve total immobilization of unconditioned animals, a treatment which constitutes a lethal psychogenic stress.

Since astronauts will be confined for long periods to very small environments which permit only a minimum of gross bodily movements, e.g., walking, it is desirable to evaluate the effect of such restriction on gastrointestinal absorption efficiency, motility, flatulence, enzyme kinetics, and tissue mass.

Since isometric type exercise has been suggested as a suitable method for preventing minerolomuscular disturbances in extended space excursions, it would also be advantageous to determine its influence on gastrointestinal function.

RADIATION

There are three known sources of ionizing radiation existing in interplanetary space which constitute a potential radiation hazard for manned space flight: the Van Allen Belt radiations, the galactic cosmic radiation, and the solar cosmic radiation. Of these three categories, the sporadic but intense solar-proton radiations present the major hazard to man. During the last solar cycle there were about six solar flare events which would have exposed a space traveler to serious radiation from solar particles (115). Numerous authors have discussed the possible effects of space radiation on biologic systems (116,117), and the subject has been reviewed by Schaefer (118). Estimates of radiation levels to be encountered in near and distant space are continually being revised (119-126) through rocket and satellite studies. However, in spite of rapid progress in this area, space radiation still constitutes an unknown factor in manned spaceflight, especially in regard to human hazards during extended flights.

The influence of radiation on gastrointestinal function and pathology has long been a subject of experimental investigation. In general, the gastrointestinal symptoms of radiation sickness constitute some of the primary acute responses to intense, acute irradiation, and depending upon the radiation characteristics, may constitute the main etiologic factors in the death of the animal. The great sensitivity of the gastrointestinal tract to intense, acute exposures to radiation is related in part to the rapid cell renewal and turnover rate of the intestinal mucosa, which, if halted, allows severe water, electrolyte (127), and blood (128) loss into the intestinal lumen, and creates a convenient site for bacterial invasion (129). Turnover rates of 1-5 days are observed for the mucous epithelial cells under normal conditions in man and animals (130). X-irradiation can abolish mitotic activity (130-134) and DNA synthesis (135) in the intestinal crypts, and can inhibit passage of cells up the villi. In addition to, and in some cases as a result of cellular mitotic changes induced by irradiation, ulcers (136-144), fistulae and strictures (145), carcinoma (146,147), and scleroses (148) of the gastrointestinal tract can be caused by irradiation. Conard (149) and Bond (150) have reviewed the effects of ionizing radiation on the physiology of the gastrointestinal tract. In brief, reports have indicated that irradiation delays gastric emptying but increases intestinal motility (151-154), decreases gastric acid secretion (155-157), decreases intestinal absorption of pyridoxine (158-159), thiamine (160), sugar (161), iron (162), N-methylnicotinamide (163), fat (164) but increases intestinal absorption of vitamin A (165).

Although the gastrointestinal effects of acute irradiation have been investigated to some extent, as indicated above, the effects of chronic and low dose exposure (conditions more similar to space hazards) on the gastrointestinal tract have not been thoroughly evaluated. Early studies (166) have shown that intestinal radiation death is not necessarily acute, and that chronic radiation reactions are known to lead to intestinal stenosis and, occasionally, to death. Hueper and De Carvajal-Forero (167) reported that repeated x-irradiation (20 exposures) of the gastric region of dogs with small doses (300r) resulted in perforating ulcers in four weeks. Recently Sullivan et al. (168) failed to find significant intestinal damage in rats given daily oral administration of yttrium-90. Thus, more information in regard to chronic, low dose irradiation effects on gastrointestinal physiology is desirable prior to extended space voyages. In addition, the space radiation hazard is complicated by 1, the unpredictability of solar flares, 2, the problem and expense of "weight trade-offs" for boosting heavy radiation shields into orbit, 3, the toxic side effects of most antiradiation drugs, and 4, the lack of dosimetry data and knowledge of biological effects of cosmic and Van Allen Belt radiation.

SUMMARY

The present review outlines the new area of endeavor, space gastroenterology, which is emerging as a distinct area of concern in the discipline of aerospace medicine. Space gastroenterology is primarily an experimental and preventive medical science dealing with problems of gastrointestinal physiology and pathology during extended space flights where restraint, dietary, radiation, and fatigue factors are exaggerated. The influence on gastrointestinal function and pathology of various stressors which will be encountered during space flight (vibration, G-stress, weightlessness, restraint, etc.) have been discussed. Table 1 summarizes the time of occurrence, effect, and anticipated problem of these various factors in space flight. In addition, important areas for future space gastroenterologic research have been enumerated.

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TABLE 1. SPACE FLIGHT PARAMETERS ASSOCIATED WITH GASTROINTESTINAL PHYSIOLOGY AND PATHOLOGY

Stressor or Stressful Situation	Time of Occurrence: Take-off and Reentry	Brief Flight (1-3 days)	Extended Flight (4 days - months)	Orbital Laboratory	Effect on Gastrointestinal Tract	Anticipated Problem	Prevention or Protection
Linear Acceleration	+	-	-	-	Organ rupture Hemorrhage Mucosal tearing Ulceration	Negligible	Controlled by restraint chairs and positioning Restriction of G-stress
Angular Acceleration	-	-	-	+	Nausea and vomiting ↑↓ Gastric secretion ↕ Gastric emptying	Negligible	Controlled by crew selecting and conditioning
Vibration	+	-	-	-	Diarrhea Hemorrhage Pain Nausea	Minor due to short duration	Controlled by crew selection and dampening chairs
Weightlessness	-	+	+	+	Flatulence (?) Defecation problems (?) Altered motility (?)	Negligible in short-term flights Unknown in long-term flights	Partial control by rotation or orbital laboratory No control in vehicle
Decompression	-	-	-	-	Flatulence Pain ↕ Gastric secretion ↕ Colonic motility	Negligible	Controlled by pressurized cabins and suits but inherent danger
Hypoxia	-	-	-	-	↑↓ Intestinal absorption ↕ Gastric emptying Ulcerogenesis	Negligible	Controlled by artificial atmosphere but inherent danger
Oxygen Toxicity	-	-	+	+	Ulcerogenesis associated with pulmonary emphysema and ACTH stress response	Unknown in long-term flights	Controlled by selection and optimal oxygen pressure and concentration
Heat	-	-	-	-	↕ Gastric emptying ↕ Intestinal absorption	Negligible	Controlled by thermal regulation in cabin but inherent danger
Fatigue and Psychologic Stress	-	-	+	+	↕ Gastric secretion Ulcerogenesis Nausea and vomiting Heartburn ↕ Intestinal motility	Negligible in short-term flights Unknown in long-term flights	Controlled by crew selection and conditioning and flight programming Inherent danger in extended voyages
Exercise Lack	+	+	+	+	Impaired absorption (?) Impaired gas elimination (?)	Negligible in short-term flights Unknown in long-term flights	Partially controlled by isometric exercises
Radiation	+	+	+	+	Hemorrhage and ulceration ↕ Gastric motility ↕ Intestinal motility ↕ Gastric secretion ↑↓ Intestinal absorption	Negligible in short-term flights Unknown in long-term flights	Itinerary planning and partial shielding beneficial, inherent danger in long-term flight
Feeding	-	+	+	+	Diverse pathologies from nutritional deficiencies	Design of adequate closed food cycle	Controlled by diet selection, special food containers, etc.
Egestion	-	+	+	+	- - -	Fecal reclamation in long-term flight Personal hygiene	Controlled by suit design and waste control system

+ indicates situation where stressor is present
− indicates situation where stressor is either absent or present to negligible degree
↑↓ designates increase or decrease

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